Acute Myeloid Leukemia (AML) Service

Background

Acute myeloid leukemia (AML) is a genetically heterogeneous hematological malignancy of myeloid lineage, characterized by clonal expansion of myeloid blast cells.

There are many different classes of AML and several related neoplasms which are genetically defined within the WHO guidelines (2016). The genetic drivers affect many different genes and range from single nucleotide polymorphisms (SNPs) to larger chromosomal changes. A range of cytogenetic and molecular tests are routinely offered at AWMGL for the detection and monitoring of genetic abnormalities in patients with a diagnosis of AML. Next generation sequencing (NGS) is also available upon request.

Acute promyelocytic leukemia (APL) is a clinically and genetically distinct class of leukemia that is clinically urgent due to its rapid progression to disseminated intravascular coagulation (DIC). It is characterized by the WHO through a reciprocal translocation which leads to a fusion gene by juxtaposition of the PML gene (on chromosome 15) and the RARA gene (on chromosome 17). The translocation is present in 95-98% of cases (Rashidi and Fisher, 2015) and is a diagnostic and prognostic marker of APL, which can be targeted with all-*trans* retinoic acid (ATRA) therapy.

Test information

- New or query AML cases will receive a diagnostic screen consisting of:
    - G-band analysis for the detection of cytogenetic abnormalities.
    - Molecular analysis for the detection of
        - CBFB-MYHII gene fusion transcripts A, D and E.
        - RUNX1-RUNX1T1 gene transcript.
        - FLT3-ITD mutation
        - FLT3 tyrosine kinase domain (FLT3-TKD) mutations
        - NPM1 mutations

- MRD testing by quantitative PCR is available for patients with a confirmed CBFB-MYHII/ RUNX1-RUNX1T1 gene fusion.

- New and query **APL cases** will be tested by rapid fluorescent in situ hybridisation (FISH) in addition to molecular testing for the PML-RARA fusion rearrangement. The PCR test is used for identification of three isoforms of the PML-RARA fusion transcript. The appropriate PCR test for that transcript may then be used for MRD testing to follow up response to treatment.

- **Next generation sequencing (NGS)** is available upon request for confirmed cases of AML.

Referral Criteria

All requests should be made on an appropriate request form available at the AWMGS website www.medicalgenomicswales.co.uk.

References

Arber, D.A., Orazi, A., Hasserjian, R., Thiele, J., Borowitz, M.J., Le Beau, M.M., Bloomfield, C.D., Cazzola, M. and Vardiman, J.W. (2016). The 2016 revision to the World Health Organization classification of myeloid

neoplasms and acute leukemia. *Blood*, [online] 127(20), pp.2391–405. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27069254/.

Rashidi, A, and S I Fisher. "FISH-Negative, Cytogenetically Cryptic Acute Promyelocytic Leukemia." *Blood Cancer Journal*, vol. 5, no. 6, June 2015, pp. e320–e320, 10.1038/bcj.2015.47.

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Sample Requirements

Bone Marrow/Peripheral Blood (Bone marrow is preferred). If possible, send a minimum of 3mL in sterile transport medium (supplied by the laboratory) or in a lithium heparin blood tube

3mL Bone Marrow/Peripheral Blood in EDTA for molecular analysis

Please label samples with three identifiers and date of collection
All samples must be accompanied by a completed request form
Consent for testing and sample storage is assumed when the request is received – it is the responsibility of the referring clinician to ensure that appropriate consent has been

TAT (Calendar days)	
G-band analysis	7 CD
FISH for new APL	3 CD
FLT3-ITD & NPM1 mutations	5 CD
FLT3-TKD mutation	10 CD
Fusion transcripts screens	14 CD
NGS	14 CD